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EXAMINER	
FORMAN, BETTY J	

ART UNIT	PAPER NUMBER
1634	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/613,006	SCHENA, MARK A.	
	Examin r	Art Unit	
	BJ Forman	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 September 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *28-46* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5/03* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 5 September 2003 has been entered.

Status of the Claims

2. This action is in response to papers filed 5 September 2003 in which claim 28 was amended. All of the amendments have been thoroughly reviewed and entered. The previous rejections in the Office Action dated 5 June 2003, not reiterated below, are withdrawn in view of the amendments and new grounds of rejection. All of the arguments have been thoroughly reviewed and are discussed below as they relate to the instant rejections. New grounds for rejection are discussed.

Claims 1-27 are cancelled.

Claims 28-48 are under prosecution.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 28-33, 36-39, 41-43 and 46 are rejected under 35 U.S.C. 102(b) as being anticipated by Gilles et al (Nature Biotechnology, April 1999, 17: 365-370).

Regarding Claim 28, Gilles et al disclose a method of simultaneously genotyping multiple samples in a single round of hybridization comprising: incubating a microarray of polynucleotide samples from multiples individuals with a probe mixture of oligonucleotides of known sequence wherein the microarray contains a plurality of samples containing genotypes of interest with each sample in a distinct location wherein each sample has polynucleotides with a defined segment containing a marker selected from a marker for a gene and markers for one or more allelic variants of the gene, the oligonucleotides in the probe mixture consist of oligonucleotides of known sequence and length and having sequences specifically complementary to those within the defined segments for each sample for which the genotype is to be determined (page 365-page 366 and Fig. 1) wherein the oligonucleotides complementary to the polynucleotides are complementary to a segment containing the marker for a gene and one or more allelic variants of the gene and a control (page 365, last line-page 366, first paragraph), the incubating forms hybrids of polynucleotides of the array and complementary oligonucleotides and allows discrimination at a single nucleotide resolution and detecting stable hybrids formed during the incubation wherein a hybridization signal indicating the formation of the hybrid after a single round of hybridization at the distinct location is indicative of a genotype of the individual (page 366, right column).

Regarding Claim 29, Gilles et al disclose the method wherein the polynucleotide samples of the microarray are amplification products (page 369, right column second and third full paragraphs).

Regarding Claim 30, Gilles et al disclose the method wherein the amplification products are produced by a PCR method (page 369, right column second and third full paragraphs).

Regarding Claim 31, Gilles et al disclose the method wherein the plurality of sample is at least 10 (page 368, left column last paragraph-page 369, first paragraph).

Regarding Claim 32, Gilles et al disclose the method wherein an allele is associated with a disease (i.e. MBP and immunological defect, page 365, left column last paragraph).

Regarding Claim 33, Gilles et al disclose the method wherein the disease is a human disease (i.e. MBP and immunological defect, page 365, left column last paragraph).

Regarding Claim 36, Gilles et al disclose the method wherein the probe mixture comprises oligonucleotides with ten different sequences (page 366, Fig. 1).

Regarding Claim 37, Gilles et al disclose the method wherein the oligonucleotides in the mixture are between about 10 and 30 nucleotides in length (page 366, Fig. 1)

Regarding Claim 38, Gilles et al disclose the method wherein the distinct segment is between about 40 and 1000 nucleotides (page 366, Fig. 1).

Regarding Claim 39, Gilles et al disclose the method wherein incubating is in an aqueous solution comprising salts and detergent (page 370, left column).

Regarding Claim 41, Gilles et al disclose the method wherein the oligonucleotides of known sequence are labeled (page 366, first paragraph).

Regarding Claim 42, Gilles et al disclose the method wherein the label is fluorescent (page 366, first paragraph).

Regarding Claim 43, Gilles et al disclose the method wherein sample from homozygous and heterozygous are distinguishable (page 368, Fig. 4).

Regarding Claim 46, Gilles et al disclose the method wherein the individual is human (page 366, left column, last paragraph).

5. Claims 28-34, 36-39, 41-42 and 46 are rejected under 35 U.S.C. 102(b) as being anticipated by Shuber (U.S. Patent No. 5,834,181, issued 10 November 1998).

Regarding Claim 28, Shuber discloses a method of simultaneously genotyping multiple samples in a single round of hybridization comprising: incubating a microarray of polynucleotide samples from multiples individuals with a probe mixture of oligonucleotides of known sequence wherein the microarray contains a plurality of samples containing genotypes of interest with each sample in a distinct location (e.g. Column 13, lines 55-63; Example 2 and Fig. 14) each sample has polynucleotides with a defined segment containing a marker selected from a marker for a gene and markers for one or more allelic variants of the gene, the oligonucleotides in the probe mixture consist essentially of oligonucleotides of known sequence and length and having sequences specifically complementary to those within the defined segments for each sample for which the genotype is to be determined wherein the oligonucleotides complementary to the polynucleotides are selected from those with sequences complementary to a segment containing the marker for a gene, one or more allelic variants of the gene and the gene and one or more allelic variants of the gene (Columns 15-19) the incubating forms hybrids of polynucleotides of the array and complementary oligonucleotides (Column 20, lines 16-44)and allows discrimination at a single nucleotide resolution (i.e. detects point mutations, Column 15, lines 32-33) and detecting stable hybrids formed during the

incubation wherein the formation of a hybrid after a single round of hybridization is indicative of a genotype (i.e. allele-specific identification, Example 2) wherein the detection of the hybridization signal is indicative of genotype (Column 25, lines 10-24).

Regarding Claim 29, Shuber discloses the method wherein the polynucleotide samples of the microarray are amplification products (Column 15-18, Tables 1-8).

Regarding Claim 30, Shuber discloses the method wherein the amplification products are produced by a PCR method (Column 12, lines 22-47 and Example 2).

Regarding Claim 31, Shuber discloses the method wherein the plurality of sample is at least 10 (Column 13, lines 55-61 and Example 2).

Regarding Claim 32, Shuber discloses the method wherein an allele is associated with a disease (e.g. cystic fibrosis, Example 2, Column 18, line 53-Column 19, line 55).

Regarding Claim 33, Shuber discloses the method wherein the disease is a human disease (e.g. cystic fibrosis, Example 2, Column 18, line 53-Column 19, line 55).

Regarding Claim 34, Shuber discloses the method wherein the disease is selected from the group consisting of β-globin, Cystic Fibrosis Transmembrane Conductance Regulator (CFTR), and Galactose-! -phosphate Uridyltransferase (Gal-1-PU) (Column 14, lines 44-51.

Regarding Claim 36, Shuber discloses the method wherein the probe mixture comprises oligonucleotides with ten different sequences (Column 18, line 53-Column 19, line 55).

Regarding Claim 37, Shuber discloses the method wherein the oligonucleotides in the mixture are between about 10 and 30 nucleotides in length (i.e. 17-mers, Example 2, Column 18, line 53-Column 19, line 55).

Regarding Claim 38, Shuber discloses the method wherein the distinct segment is between about 40 and 1000 nucleotides (Column 12, lines 30-37).

Regarding Claim 39, Shuber discloses the method wherein incubating is in an aqueous solution comprising salts and detergent (e.g. EDTA & SDS, Column 20, lines 17-22).

Regarding Claim 41, Shuber discloses the method wherein the oligonucleotides of known sequence are labeled (Column 20, lines 1-15).

Regarding Claim 42, Shuber discloses the method wherein the label is fluorescent (Column 25, lines 11-24).

Regarding Claim 46, Shuber discloses the method wherein the individual is human (Example 2).

Response to Arguments

6. Applicant argues that Shuber teaches do not teach determination of genotype by detecting a hybridization signal, but instead interrogates the oligonucleotide sequence. The argument has been considered but is not found persuasive because, as noted above, Shuber does teach genotype determination by hybridization signal detection (Column 25, lines 12-24). Therefore, Shuber teaches the method as claimed.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 32-34 and 45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gilles et al (Nature Biotechnology, April 1999, 17: 365-370) in view of Shuber et al (U.S. Patent No. 5,834,181, issued 10 November 1998).

Regarding Claims 32-34, Gilles et al disclose a method of simultaneously genotyping multiple samples in a single round of hybridization comprising: incubating a microarray of polynucleotide samples from multiples individuals with a probe mixture of oligonucleotides of known sequence wherein the microarray contains a plurality of samples containing genotypes of interest with each sample in a distinct location wherein each sample has polynucleotides with a defined segment containing a marker selected from a marker for a gene and markers for one or more allelic variants of the gene, the oligonucleotides in the probe mixture consist of oligonucleotides of known sequence and length and having sequences specifically complementary to those within the defined segments for each sample for which the genotype is to be determined (page 365-page 366 and Fig. 1) wherein the oligonucleotides complementary to the polynucleotides are complementary to a segment containing the marker for a gene and one or more allelic variants of the gene and a control (page 365, last line-page 366, first paragraph), the incubating forms hybrids of polynucleotides of the array and complementary oligonucleotides and allows discrimination at a single nucleotide resolution and detecting stable hybrids formed during the incubation wherein a hybridization signal indicating the formation of the hybrid after a single round of hybridization at the distinct location is indicative of a genotype of the individual (page 366, right column). Gilles et al teach the allele is "associated" with disease, but they do not teach the allele is associated with the claimed specific diseases.

Shuber teaches a similar method of simultaneously genotyping multiple samples in a single round of hybridization comprising: incubating a microarray of polynucleotide samples from multiples individuals with a probe mixture of oligonucleotides of known sequence wherein the microarray contains a plurality of samples containing genotypes of interest with each

sample in a distinct location (e.g. Column 13, lines 55-63; Example 2 and Fig. 14) each sample has polynucleotides with a defined segment containing a marker selected from a marker for a gene and markers for one or more allelic variants of the gene, the oligonucleotides in the probe mixture consist essentially of oligonucleotides of known sequence and length and having sequences specifically complementary to those within the defined segments for each sample for which the genotype is to be determined wherein the oligonucleotides complementary to the polynucleotides are selected from those with sequences complementary to a segment containing the marker for a gene, one or more allelic variants of the gene and the gene and one or more allelic variants of the gene (Columns 15-19) the incubating forms hybrids of polynucleotides of the array and complementary oligonucleotides (Column 20, lines 16-44)and allows discrimination at a single nucleotide resolution (i.e. detects point mutations, Column 15, lines 32-33) and detecting stable hybrids formed during the incubation wherein the formation of a hybrid after a single round of hybridization is indicative of a genotype (i.e. allele-specific identification, Example 2) wherein the allele is associated with a human disease selected from the group consisting of β-globin, Cystic Fibrosis Transmembrane Conductance Regulator (CFTR), and Galactose-! -phosphate Uridyltransferase (Gal-1-PU) (Column 14, lines 44-51. Shuber further teaches that their method provides high-throughput detection and identification of genetic diseases (Column 1, lines 13-24). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the allele detection of Gilles et al by detecting the specific disease-specific alleles taught by Shuber for the expected benefit of detecting disease-specific alleles rapidly and specifically as taught by Shuber (Column 2, lines 28-33).

Regarding Claim 45, Shuber further teaches the method wherein the samples are prenatal blood samples (Column 6, lines 13-19) but they do not specifically teach the blood samples are neonatal.

However, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the diagnostic array comprising prenatal blood samples taught by Shuber to comprise samples from neonatal blood for the obvious benefits of prenatal diagnosis i.e. by detecting the presence of mutant genes in neonatal samples, the disease maybe prevented and/or treated as early as possible.

9. Claims 35 and 44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gilles et al (Nature Biotechnology, April 1999, 17: 365-370) in view of Brown et al (U.S. Patent No. 5,807,522, issued 15 September 1998).

Regarding Claims 35 and 44, Gilles et al disclose a method of simultaneously genotyping multiple samples in a single round of hybridization comprising: incubating a microarray of polynucleotide samples from multiples individuals with a probe mixture of oligonucleotides of known sequence wherein the microarray contains a plurality of samples containing genotypes of interest with each sample in a distinct location wherein each sample has polynucleotides with a defined segment containing a marker selected from a marker for a gene and markers for one or more allelic variants of the gene, the oligonucleotides in the probe mixture consist of oligonucleotides of known sequence and length and having sequences specifically complementary to those within the defined segments for each sample for which the genotype is to be determined (page 365-page 366 and Fig. 1) but they are silent regarding the number of locations/cm^2 and the number of possible polynucleotide samples.

However, Brown et al teach a similar method comprising: incubating a microarray of polynucleotide samples from multiples individuals with a probe mixture of oligonucleotides of

known sequence wherein the microarray contains a plurality of samples containing genotypes of interest with each sample in a distinct location wherein each sample has polynucleotides with a defined segment containing a marker selected from a marker for a gene and markers for one or more allelic variants of the gene (Column 15, lines 19-51) wherein the microarray comprises at least 1000 locations/cm^2 (Column 6, lines 32-38) and wherein the microarray is 3cmx3cm (Column 5, lines 63-67 and Fig. 12) thereby providing the at least 5,000 polynucleotide samples as claimed.

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the 1000 locations/cm^2 and 5,000 polynucleotide samples taught by Brown et al to the microarray of Gilles et al thereby providing a microarray for large scale screening assays as taught by Brown et al (Column 1, lines 15-19) for the expected benefit of rapid and convenient screening of large number of samples as taught by Brown et al (Column 15, lines 52-67).

10. Claim 40 is rejected under 35 U.S.C. 103(a) as being unpatentable over Gilles et al (Nature Biotechnology, 1999, 17: 365-370).in view of Hames et al (Nucleic Acid Hybridization: a practical approach, IRL Press, Washington DC, 1985, pages 105-108).

Regarding Claim 40, Gilles et al disclose a method of simultaneously genotyping multiple samples in a single round of hybridization comprising: incubating a microarray of polynucleotide samples from multiples individuals with a probe mixture of oligonucleotides of known sequence wherein the microarray contains a plurality of samples containing genotypes of interest with each sample in a distinct location wherein each sample has polynucleotides

with a defined segment containing a marker selected from a marker for a gene and markers for one or more allelic variants of the gene, the oligonucleotides in the probe mixture consist of oligonucleotides of known sequence and length and having sequences specifically complementary to those within the defined segments for each sample for which the genotype is to be determined (page 365-page 366 and Fig. 1) but they are silent regarding the number of locations/cm^2 and the number of possible polynucleotide samples. Gilles is silent regarding hybridizing at about 10° C below stable hybrid melting temperature.

However it was well known in the art at the time the claimed invention was made that stable hybrids of closely related sequences are hybridized and distinguishable at about 10° C below melting temperature as taught by Hames et al (page 105 (i) and page 108, first full paragraph, lines 8-10). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the hybridization temperatures taught by Hames et al (i.e. about 10° C below melting) to the allele-specific hybridizations of Gilles because the hybridizations are designed to distinguish between closely related sequences. Therefore, one of ordinary skill in the art would have been motivated to hybridize the nucleic acids of Gilles at about 10° C below melting for the obvious benefits of distinguishing between their closely related sequences as taught by Hames et al and to thereby accurately genotype the individuals.

11. Claims 35 and 43-45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shuber (U.S. Patent No. 5,834,181, issued 10 November 1998) in view of Drmanac (U.S. Patent No. 6,025,136, filed 28 August 1997).

Regarding Claim 35, Shuber discloses a method of simultaneously genotyping multiple samples in a single round of hybridization comprising: incubating a microarray of polynucleotide samples from multiples individuals with a probe mixture of oligonucleotides of known sequence wherein the microarray contains a plurality of samples containing genotypes of interest with each sample in a distinct location (e.g. Column 13, lines 55-63; Example 2 and Fig. 14) each sample has polynucleotides with a defined segment containing a marker selected from a marker for a gene and markers for one or more allelic variants of the gene, the oligonucleotides in the probe mixture consist essentially of oligonucleotides of known sequence and length and having sequences specifically complementary to those within the defined segments for each sample for which the genotype is to be determined wherein the oligonucleotides complementary to the polynucleotides are selected from those with sequences complementary to a segment containing the marker for a gene, one or more allelic variants of the gene and the gene and one or more allelic variants of the gene (Columns 15-19) the incubating forms hybrids of polynucleotides of the array and complementary oligonucleotides (Column 20, lines 16-44)and allows discrimination at a single nucleotide resolution (i.e. detects point mutations, Column 15, lines 32-33) and detecting stable hybrids formed during the incubation wherein the formation of a hybrid after a single round of hybridization is indicative of a genotype (i.e. allele-specific identification, Example 2) wherein the surface comprises at least 1000 locations (Fig. 14) but they are silent regarding the density being 1000 locations/ cm^2 . However, array densities of 1000 locations/cm^2 were well known in the art at the time the instant invention was made as taught by Drmanac. Drmanac teaches a similar method of simultaneously genotyping multiple samples comprising: incubating a microarray of polynucleotide samples from multiple individuals with probes of a known sequence wherein the array contains a plurality of sample containing genotypes of interest with each sample in a distinct location wherein the microarray comprises at least 1000 locations/cm^2 i.e. 25/mm^2 (Column 5, lines 46-48).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the location density of Drmanac to the microarray of Shuber to thereby maximize the number of assays per hybridization as desired by Shuber (Column 5, lines 21-30). It is noted that *In re Aller*, 220 F.2d 454,456, 105 USPQ 233,235 states where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum by routine experimentation.

Regarding Claim 43, Shuber teaches the method where in the allele-specific genetic alterations are identified but they do not specifically teach that the method distinguishes homozygotes and heterzygotes. However, distinguishing between homozygotes and heterzygotes was well known and routinely practiced in the art at the time the claimed invention was made as taught by Drmanac who specifically teaches that samples from homozygotes and heterozygotes are distinguishable (Column 4, lines 7-19). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the method of Shuber to distinguishing between homozygotes and heterozygotes as taught by Drmanac based on the importance of their distinction as taught by Drmanac (Column 4, lines 7-19).

Regarding Claim 44, Shuber teaches the method wherein the plurality of samples is at least 500 (Column 5,lines 21-30) but they do not teach the samples are at least 5000. However, immobilized sample of at least 5000 were well known and routinely practiced in the art at the time the claimed invention was made as taught by Drmanac who teaches the plurality of samples is at least 5000 i.e. a subarray contains 256 samples (Column 4, lines 42-43) and the array comprises 50 subarrays (Column 3, lines 33-36).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the sample number of Drmanac to the immobilized samples of Shuber to thereby maximize the number of assays per hybridization as desired by Shuber (Column 5, lines 21-30). It is noted that *In re Aller*, 220 F.2d 454,456, 105 USPQ 233,235

states where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum by routine experimentation.

Regarding Claim 45, Shuber teaches the method wherein the samples are prenatal blood samples (Column 6, lines 13-19) but they do not specifically teach the blood samples are neonatal.

However, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the diagnostic array comprising prenatal blood samples taught by Shuber to comprise samples from neonatal blood for the obvious benefits of prenatal diagnosis i.e. by detecting the presence of mutant genes in neonatal samples, the disease maybe prevented and/or treated as early as possible.

Response to Arguments

12. Applicant argues that Shuber does not teach the method of Claim 28 and Dramanac does not cure the deficiencies of Shuber. Therefore, Applicant argues, the cited art does not teach the claimed invention. The argument has been considered but is not found persuasive for the reasons stated above i.e. Shuber does teach the method of claim 28.

13. Claim 40 is rejected under 35 U.S.C. 103(a) as being unpatentable over Shuber (U.S. Patent No. 5,834,181, issued 10 November 1998) in view of Hames et al (Nucleic Acid Hybridization: a practical approach, IRL Press, Washington DC, 1985, pages 105-108).

Regarding Claim 40, Shuber teaches the method of simultaneously genotyping multiple samples in a single round of hybridization comprising: incubating a microarray of polynucleotide samples from multiples individuals with a probe mixture of oligonucleotides of

known sequence wherein the microarray contains a plurality of samples containing genotypes of interest with each sample in a distinct location each sample has polynucleotides with a defined segment containing a marker selected from a marker for a gene and markers for one or more allelic variants of the gene, the oligonucleotides in the probe mixture consist essentially of oligonucleotides of known sequence and length and having sequences specifically complementary to those within the defined segments for each sample for which the genotype is to be determined wherein the oligonucleotides complementary to the polynucleotides are selected from those with sequences complementary to a segment containing the marker for a gene, one or more allelic variants of the gene and the gene and one or more allelic variants of the gene (Columns 15-19) the incubating forms hybrids of polynucleotides of the array and complementary oligonucleotides (Column 20, lines 16-44)and allows discrimination at a single nucleotide resolution (i.e. detects point mutations, Column 15, lines 32-33) and detecting stable hybrids formed during the incubation wherein the formation of a hybrid after a single round of hybridization is indicative of a genotype (i.e. allele-specific identification, Example 2) hybridization is performed below melting of stable hybrids (Column 20, lines 35-40) but is silent regarding hybridizing at about 10° C below stable hybrid melting temperature.

However it was well known in the art at the time the claimed invention was made that stable hybrids of closely related sequences are hybridized and distinguishable at about 10° C below melting temperature as taught by Hames et al (page 105 (i) and page 108, first full paragraph, lines 8-10). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the hybridization temperatures taught by Hames et al (i.e. about 10° C below melting) to the allele-specific hybridizations of Shuber because the hybridizations are designed to distinguish between closely related sequences. Therefore, one of ordinary skill in the art would have been motivated to hybridize the nucleic acids of Shuber at about 10° C below melting for the obvious benefits of distinguishing between their closely

related sequences as taught by Hames et al and to thereby accurately genotype the individuals.

Response to Arguments

14. Applicant argues that Shuber does not teach the method of Claim 28 and Hames does not cure the deficiencies of Shuber. Therefore, Applicant argues, the cited art does not teach the claimed invention. The argument has been considered but is not found persuasive for the reasons stated above i.e. Shuber does teach the method of claim 28.

Conclusion

15. No claim is allowed.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (703) 306-5878. The examiner can normally be reached on 6:30 TO 4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (703) 308-1119. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 308-8724 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

BJ Forman, Ph.D.
Primary Examiner
Art Unit: 1634
October 27, 2003